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To cite this version:

T. Sari, M. El Hajji, Jérôme Harmand. The mathematical analysis of a syntrophic relationship between two microbial species in a chemostat. Mathematical Biosciences and Engineering, 2012, 9 (3), p. 627 - p. 645. 10.3934/mbe.2012.9.627 . hal-00765311

HAL Id: hal-00765311

https://hal.science/hal-00765311v1

Submitted on 14 Dec 2012

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Author-produced version of the article published in Mathematical Biosciences and Engineering, 2012, 9(3), 627-645.
The original publication is available at http://aimsciences.org
Doi : 10.3934/mbe.2012.9.627

MATHEMATICAL BIOSCIENCES
AND ENGINEERING
Volume **xx**, Number **0xx**, xx **20xx**

doi:10.3934/mbe.20xx.xx.xx

pp. **1–xx**

THE MATHEMATICAL ANALYSIS OF A SYNTROPHIC RELATIONSHIP BETWEEN TWO MICROBIAL SPECIES IN A CHEMOSTAT

Abstract. A mathematical model involving a syntrophic relationship between two populations of bacteria in a continuous culture is proposed. A detailed qualitative analysis is carried out as well as the analysis of the local and global stability of the equilibria. We demonstrate, under general assumptions of monotonicity which are relevant from an applied point of view, the asymptotic stability of the positive equilibrium point which corresponds to the coexistence of the two bacteria. A syntrophic relationship in the anaerobic digestion process is proposed as a real candidate for this model.

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(Communicated by Patrick de Leenheer)

1. **Introduction.** A synthrophic relationship between two organisms refers to a situation where the species exhibit mutualism but where, in contrast to what happens in a purely symbiotic relationship, one of the species can grow without the other. Such a situation can be mathematically formalized as follows: assume that a first species denoted X_1 grows on a substrate S_1 forming an intermediate product S_2. This intermediate product is required for its growth by a second species X_2. Since the substrate needed for its growth by the second bacteria is the product of the first bioreaction, the second bacteria cannot grow if the first one is not present.

An important feature of our work is that it involves mutualism. Such an interaction is quite common in nature which explains why a number of models have already been proposed in the literature. Katsuyama *et al.* [11], describing pesticide degradation proposed a model involving two mutualistic species, while a more general case was considered by Kreikenbohm and Bohl [12]. Since mutualism generally

2000 *Mathematics Subject Classification.* Primary: 92A15, 92A17; Secondary: 34C15, 34C35.

Key words and phrases. Chemostat, Syntrophic relationship, Coexistence, Global asymptotic stability, Anaerobic digestion.

Part of this work was carried out when second author was a PhD student in the Inra/Inria team Modemic. The authors acknowledge Inra and Inria for financial support.

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involves species interacting through intermediate products, other studies have considered mutualistic relationships in food webs. For instance, Bratbak and Thingstad [3], and, more recently, Aota and Nakajima [1] have explored mutualism between phytoplankton and bacteria through carbon excretion by phytoplankton. A model studied by Freedman *et al.* [10] was proposed to explain the observed coexistence of such species. Another characteristic of the present work is that it involves several substrates. A considerable number of studies have appeared in the literature over the last years treating this subject. For a recent review of this field, the reader may refer for instance to Chase and Leibold [5] or Ballyk and Wolkowicz [2]. However, in previous studies the models have usually been very specific. In particular, the mathematical analysis of the models have been designed for specific growth rates that are explicitly given (in most cases as Monod functions).

To extend the study of mutualism to more general systems, we have recently considered more general assumptions, notably with respect to the growth rate functions considered in the models in using qualitative hypotheses, cf. [7] . Furthermore, wa have assumed that the species X_1 may be inhibited by the product S_2 that it has produced itself while the species X_2 was simply limited by S_2. An example of such interaction is anaerobic digestion in which mutualistic relationships allow certain classes of bacteria to coexist. A mutualistic relation has also been considered in [6]. See [8] for another model of coexistence in the chemostat.

In this paper, following [9], we revisit the model proposed in [7] in incorporating two main changes which significantly extend the range of practical situations covered by the model. First, we assume that there is some S_2 in the influent or, to put it differently, the limiting substrate S_2 on which the species X_2 grows is not only produced by the species X_1 but is also available even if the species X_1 is not present. The second modification to the model is that the second species is assumed to be inhibited by an excess of S_1, the limiting substrate on which the first species grows. To illustrate the usefulness of such extensions of the original model proposed by El Hajji et al. [7], the biological interpretation of these hypotheses within the context of the anaerobic process is given in the appendix.

The paper is organized as follows. In Section 2, we propose a modification of the model studied in [7] that involves four differential equations. In Section 3, the system is reduced to a planar system, for which equilibria are determined and their local stability properties established. In Section 4, when the system has a single positive equilibrium, the global asymptotic stability is demonstrated using Dulac's criterion (which rules out the possibility of the existence of periodic solutions for the reduced planar system), the Poincaré-Bendixon Theorem and the Butler-McGehee Lemma. Hence, in this case, for all positive initial conditions, the solutions converge to the positive equilibrium point which corresponds to the coexistence of the two bacterial species as observed in real processes. Application to the original model in [7] is given in Section 5. In this section, numerical simulations are presented in the case when the growth functions are of the Monod type. Concluding remarks are given in Section 6. An example of a syntrophic relationship is given in Appendix A as a candidate for this model. The mathematical proofs of the results are given in Appendix B.

2. **Mathematical model.** Let S_1, X_1, S_2 and X_2 denote, respectively, the concentrations of the substrate, the first bacteria, the intermediate product, and the second bacteria present in the reactor at time t. We neglect all species-specific death

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rates and take into account the dilution rate only. Hence our model is described by the following system of ordinary differential equations :

$$\begin{cases} \dot{S}_1 &= D(S_1^{in} - S_1) - k_3\mu_1(S_1, S_2)X_1 \ , \\ \dot{X}_1 &= \mu_1(S_1, S_2)X_1 - DX_1 \ , \\ \dot{S}_2 &= D(S_2^{in} - S_2) - k_2\mu_2(S_1, S_2)X_2 + k_1\mu_1(S_1, S_2)X_1 \ , \\ \dot{X}_2 &= \mu_2(S_1, S_2)X_2 - DX_2 \ . \end{cases} \tag{1}$$

where $S_1^{in} > 0$ denotes the input concentration of substrate, $S_2^{in} > 0$ the input concentration of the intermediate product and $D > 0$ the dilution rate.

Assume that the functional response of each species $\mu_1, \mu_2 : \mathbb{R}_+^2 \to \mathbb{R}_+$ satisfies :

A1: $\mu_1, \mu_2 : \mathbb{R}_+^2 \to \mathbb{R}_+$, of class $\mathcal{C}^1$,

A2: For all $(S_1, S_2) \in \mathbb{R}_+^2$, $\mu_1(0, S_2) = 0$ and $\mu_2(S_1, 0) = 0$.

A3: For all $(S_1, S_2) \in \mathbb{R}_+^2$, $\dfrac{\partial \mu_1}{\partial S_1}(S_1, S_2) > 0$ and $\dfrac{\partial \mu_1}{\partial S_2}(S_1, S_2) < 0$

A4: For all $(S_1, S_2) \in \mathbb{R}_+^2$, $\dfrac{\partial \mu_2}{\partial S_1}(S_1, S_2) \leq 0$ and $\dfrac{\partial \mu_2}{\partial S_2}(S_1, S_2) > 0$.

Hypothesis **A2** signifies that no growth can take place for species X_1 without the substrate S_1 and that the intermediate product S_2 is necessary for the growth of species X_2. Hypothesis **A3** means that the growth of species X_1 increases with the substrate S_1 but it is inhibited by the intermediate product S_2 that it produces. Hypothesis **A4** means that the growth of species X_2 increases with intermediate product S_2 produced by species X_1 while it is inhibited by the substrate S_1. Note that there is a syntrophic relationship between the two species.

We first scale system (1) using the following change of variables and notations :

$$s_1 = \frac{k_1}{k_3}S_1, \quad x_1 = k_1X_1, \quad s_2 = S_2, \quad x_2 = k_2X_2, \quad s_1^{in} = \frac{k_1}{k_3}S_1^{in}, \quad s_2^{in} = S_2^{in} \ .$$

Thus, the dimensionless equations obtained are :

$$\begin{cases} \dot{s}_1 &= D(s_1^{in} - s_1) - f_1(s_1, s_2)x_1 \ , \\ \dot{x}_1 &= f_1(s_1, s_2)x_1 - Dx_1 \ , \\ \dot{s}_2 &= D(s_2^{in} - s_2) - f_2(s_1, s_2)x_2 + f_1(s_1, s_2)x_1 \ , \\ \dot{x}_2 &= f_2(s_1, s_2)x_2 - Dx_2 \ . \end{cases} \tag{2}$$

Where the functions $f_1, f_2 : \mathbb{R}_+^2 \to \mathbb{R}_+$ are defined by

$$f_1(s_1, s_2) = \mu_1(\frac{k_3}{k_1}s_1, s_2) \quad \text{and} \quad f_2(s_1, s_2) = \mu_2(\frac{k_3}{k_1}s_1, s_2).$$

Since the functions μ_1 and μ_2 satisfy hypostheses **A1**–**A4**, it follows that functions f_1 and f_2 satisfy

H1: $f_1, f_2 : \mathbb{R}_+^2 \to \mathbb{R}_+$, of class $\mathcal{C}^1$,

H2: For all $(s_1, s_2) \in \mathbb{R}_+^2$, $f_1(0, s_2) = 0$ and $f_2(s_1, 0) = 0$.

H3: For all $(s_1, s_2) \in \mathbb{R}_+^2$, $\dfrac{\partial f_1}{\partial s_1}(s_1, s_2) > 0$ and $\dfrac{\partial f_1}{\partial s_2}(s_1, s_2) < 0$.

H4: For all $(s_1, s_2) \in \mathbb{R}_+^2$, $\dfrac{\partial f_2}{\partial s_1}(s_1, s_2) \leq 0$ and $\dfrac{\partial f_2}{\partial s_2}(s_1, s_2) > 0$.

$\mathbb{R}_+^4$, the closed non-negative cone in $\mathbb{R}^4$, is positively invariant under the solution map of system (2). More precisely

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Doi : 10.3934/mbe.2012.9.627

Proposition 1. *For every initial condition in $\mathbb{R}^4_+$, the solution of system (2) has positive components and is positively bounded and thus is defined for every positive t. The set*

$$\Omega = \left\{(s_1, x_1, s_2, x_2) \in \mathbb{R}^4_+ : \; s_1 + x_1 = s_1^{in}, \quad s_2 + x_2 = x_1 + s_2^{in}\right\}$$

is a positive invariant attractor of all solutions of system (2).

3. **Restriction on the plane.** The solutions of system (2) are exponentially convergent towards the set Ω and we are interested in the asymptotic behavior of these solutions. It is enough to restrict the study of the asymptotic behaviour of system (2) to Ω. In fact, thanks to Thieme's results [14], the asymptotic behaviour of the solutions of the restriction of (2) on Ω will be informative for the complete system (see Section 4). In this section, we study the following reduced system which is simply the projection on the plane (x_1, x_2), of the restriction of system (2) on Ω.

$$\begin{cases} \dot{x}_1 = [\Phi_1(x_1, x_2) - D]\, x_1, \\ \dot{x}_2 = [\Phi_2(x_1, x_2) - D]\, x_2. \end{cases} \tag{3}$$

where

$$\Phi_1(x_1, x_2) = f_1\left(s_1^{in} - x_1, s_2^{in} + x_1 - x_2\right),$$
$$\Phi_2(x_1, x_2) = f_2\left(s_1^{in} - x_1, s_2^{in} + x_1 - x_2\right).$$

Thus, for (3) the state-vector (x_1, x_2) belongs to the following subset of the plane as illustrated in Fig. 1:

$$\mathcal{S} = \left\{(x_1, x_2) \in {\mathbb{R}_+}^2 : 0 < x_1 \leq s_1^{in}, 0 < x_2 \leq x_1 + s_2^{in}\right\}.$$

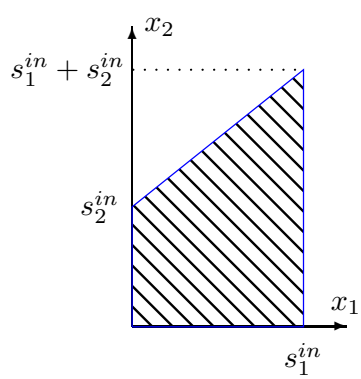

FIGURE 1. The set $\mathcal{S}$

The point $F^0 = (0, 0)$ is an equilibrium of (3). Besides this equilibrium point the system can have the following three types of equilibrium points:

- Boundary equilibria $F^1 = (\bar{x}_1, 0)$, where $x_1 = \bar{x}_1$ is a solution, if it exists, of the equation
$$\Phi_1(x_1, 0) = D, \tag{4}$$
- Boundary equilibria $F^2 = (0, \tilde{x}_2)$, where $x_2 = \tilde{x}_2$ is a solution, if it exists, of the equation
$$\Phi_2(0, x_2) = D, \tag{5}$$

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- Positive equilibria $F^* = (x_1^*, x_2^*)$, where $x_1 = x_1^*$, $x_2 = x_2^*$ is a solution, if it exists, of the system of equations

$$\begin{cases} \Phi_1(x_1, x_2) = D \\ \Phi_2(x_1, x_2) = D. \end{cases} \tag{6}$$

We use the following notations

$$D_1 = f_1(s_1^{in}, s_2^{in}), \qquad D_2 = f_2(s_1^{in}, s_2^{in}). \tag{7}$$

The mapping $x_1 \mapsto \Phi_1(x_1, 0)$ is decreasing, and the mapping $x_1 \mapsto \Phi_2(x_1, 0)$ is increasing as in Figure 2. If $D_1 < D_2$, there is no real number ξ_1 satisfying $\Phi_1(\xi_1, 0) = \Phi_2(\xi_1, 0)$: see Figure 2, left. If $D_1 > D_2$, there exists a sole real number ξ_1 satisfying $\Phi_1(\xi_1, 0) = \Phi_2(\xi_1, 0)$, since

$$\Phi_1(0, 0) = D_1 > D_2 = \Phi_2(0, 0), \text{ and } \Phi_1(s_1^{in}, 0) = 0 < \Phi_2(s_1^{in}, 0).$$

We denote by $D_3 \in]D_2, D_1[$ the unique real number (see Figure 2, right) such that:

$$\Phi_1(\xi_1, 0) = \Phi_2(\xi_1, 0) = D_3. \tag{8}$$

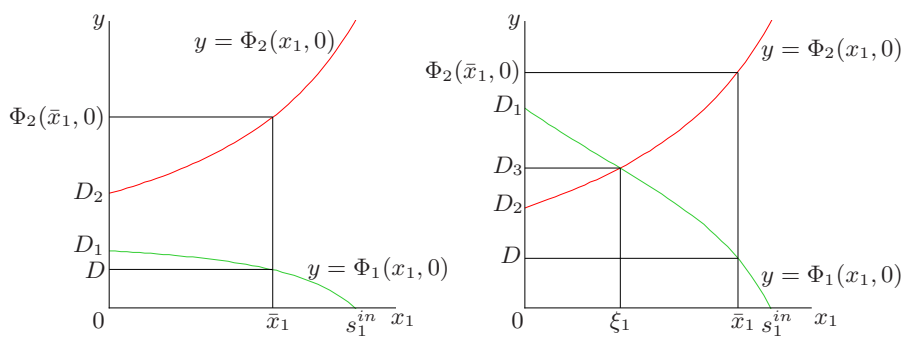

FIGURE 2. Existence and uniqueness of $\bar{x}_1$. On the left, the case $D_1 < D_2$: $\Phi_2(\bar{x}_1, 0) > D$ for all $D < D_1$. On the right, the case $D_1 > D_2$: $\Phi_2(\bar{x}_1, 0) > D$ if and only if $D < D_3$.

The mapping $x_2 \mapsto \Phi_1(0, x_2)$ is increasing, and the mapping $x_2 \mapsto \Phi_2(0, x_2)$ is decreasing: see Figure 3. if $D_1 > D_2$, there is no real number ξ_2 satisfying $\Phi_1(0, \xi_2) = \Phi_2(0, \xi_2)$, see Figure 3, left. If $D_1 < D_2$, there exists a single real number ξ_2 satisfying $\Phi_1(0, \xi_2) = \Phi_2(0, \xi_2)$, since

$$\Phi_2(0, 0) = D_2 > D_1 = \Phi_1(0, 0), \text{ and } \Phi_2(0, s_2^{in}) = 0 < \Phi_1(0, s_2^{in}).$$

We denote by $D_4 \in]D_1, D_2[$ the sole real number (see Figure 3, right) such that:

$$\Phi_1(0, \xi_2) = \Phi_2(0, \xi_2) = D_4.$$

The nature of the trivial equilibrium point F^0 is given in the following lemma.

Lemma 1. *If $D > \max(D_1, D_2)$, then F^0 is a stable node. If $\min(D_1, D_2) < D < \max(D_1, D_2)$, then F^0 is a saddle point. If $D < \min(D_1, D_2)$, then F^0 is an unstable node.*

The conditions of existence of the boundary equilibria F^1 and F^2, and their nature, are stated in the following lemmas.

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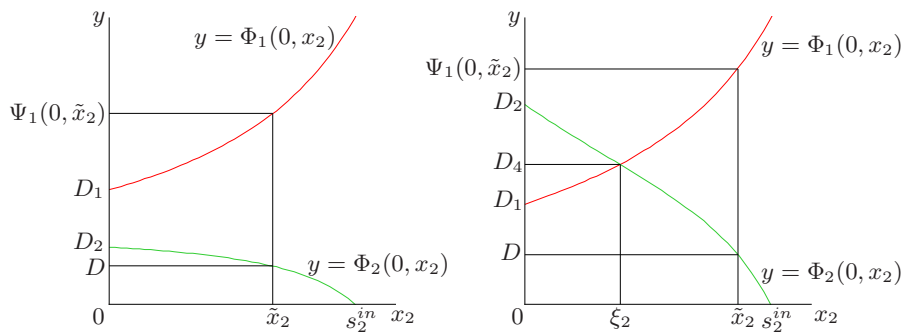

FIGURE 3. Existence and uniqueness of $\tilde{x}_2$. On the left, the case $D_2 < D_1$: $\Phi_1(0, \tilde{x}_2) > D$ for all $D < D_2$. On the right, the case $D_2 > D_1$: $\Phi_1(0, \tilde{x}_2) > D$ if and only if $D < D_4$.

Lemma 2. *An equilibrium $F^1 = (\bar{x}_1, 0)$ exists if and only if $D < D_1$. If it exists, then it the sole equilibrium on the positive x_1 semi-axis. If $D_1 < D_2$, then F^1 is a saddle point for all $D < D_1$. If $D_2 < D_1$, then F^1 is a saddle point for all $0 < D < D_3$ and a stable node for all $D_3 < D < D_1$.*

Lemma 3. *An equilibrium $F^2 = (0, \tilde{x}_2)$ exists if and only if $D < D_2$. If it exists, then it the sole equilibrium on the positive x_2 semi-axis. If $D_2 < D_1$, then F^2 is a saddle point for all $D < D_2$. If $D_1 < D_2$, then F^2 is a saddle point for all $0 < D < D_4$ and a stable node for all $D_4 < D < D_2$.*

Let us now discuss the conditions of existence of positive equilibria F^* and their number. An equilibrium $F^* = (x_1^*, x_2^*)$ exists if and only if $x_1 = x_1^*$, $x_2 = x_2^*$ which is a solution of (6) lying in $\mathcal{S}$. this gives

$$\frac{\partial \Phi_1}{\partial x_2} = -\frac{\partial f_1}{\partial s_2}(s_1^{in} - x_1, s_2^{in} + x_1 - x_2).$$

Assuming **H3** is satisfied, this partial derivative is positive. Hence, equation

$$\Phi_1(x_1, x_2) = D$$

defines a function $x_2 = F_1(x_1)$ such that $F_1(\bar{x}_1) = 0$ when $D < D_1$. Recall that $x_1 = \bar{x}_1$ is the solution of (4) which, according to Lemma 2, exists and is unique, if and only if $D < D_1$. This gives

$$F_1'(x_1) = -\frac{\frac{\partial \Phi_1}{\partial x_1}(x_1, F_1(x_1))}{\frac{\partial \Phi_1}{\partial x_2}(x_1, F_1(x_1))} = \frac{-\frac{\partial f_1}{\partial s_1} + \frac{\partial f_1}{\partial s_2}}{\frac{\partial f_1}{\partial s_2}} = 1 - \frac{\frac{\partial f_1}{\partial s_1}}{\frac{\partial f_1}{\partial s_2}} > 1.$$

Hence the function F_1 is increasing. Since $\Phi_1(s_1^{in}, 0) = 0$, the graph Γ_1 of F_1 has no intersection with the right boundary of the domain $\mathcal{S}$, defined by $x_1 = s_1^{in}$. This graph separates $\mathcal{S}$ in two regions denoted as the left and right sides of Γ_1: see Figure 4. This also gives

$$\frac{\partial \Phi_2}{\partial x_2} = -\frac{\partial f_2}{\partial s_2}(s_1^{in} - x_1, s_2^{in} + x_1 - x_2).$$

By assuming **H4**, this partial derivative is positive. Hence, equation $\Phi_2(x_1, x_2) = D$ defines a function $x_2 = F_2(x_1)$ such that $F_2(0) = \tilde{x}_2$ when $D < D_2$. Recall that

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$x_2 = \tilde{x}_2$ is the solution of (5) which, according to Lemma 3 exists and is unique, if and only if $D < D_2$. This gives

$$F_2'(x_1) = -\frac{\frac{\partial \Phi_2}{\partial x_1}(x_1, F_2(x_1))}{\frac{\partial \Phi_2}{\partial x_2}(x_1, F_2(x_1))} = \frac{-\frac{\partial f_2}{\partial s_1} + \frac{\partial f_2}{\partial s_2}}{\frac{\partial f_2}{\partial s_2}} = 1 - \frac{\frac{\partial f_2}{\partial s_1}}{\frac{\partial f_2}{\partial s_2}} > 1.$$

Hence the function F_2 is increasing. Since $\Phi_2(x_1, s_2^{in} + x_1) = 0$, the graph Γ_2 of F_2 has no intersection with the top boundary of the domain $\mathcal{S}$, defined by $x_2 = s_2^{in} + x_1$. Thus the point at the very right of Γ_2 lies necessarily on the right boundary of $\mathcal{S}$, defined by $x_1 = s_1^{in}$. Hence it lies on the right side of Γ_1: see Figure 4.

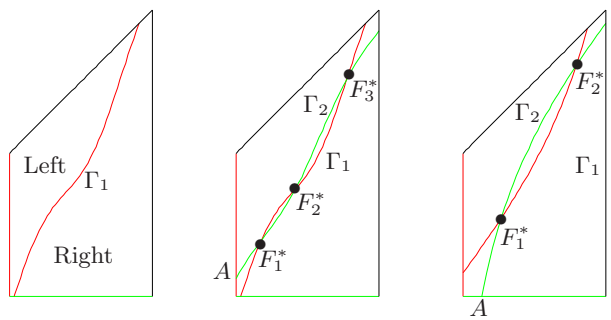

FIGURE 4. On the left, the left and right sides of Γ_1. In the center, the point A at the very left of Γ_2 lies on left side of Γ_1: there are generically an odd number of intersections (3 in this example). On the right, the point A at the very left of Γ_2 lies on right side of Γ_1: there are generically an even number of intersections (2 in this example).

The graphs Γ_1 and Γ_2 can intersect or not (see Figures 4, 6 and 7). If they intersect at some point $F^* = (x_1^*, x_2^*)$ then F^* is a positive equilibrium. If the point A at the very left of Γ_2 lies on left side of Γ_1 then Γ_1 and Γ_2 intersect in at least one point $F^* = (x_1^*, x_2^*)$. They can have multiple intersections. Generically, they have an odd number of intersections (see Figure 4, center). If the point A at the very left of Γ_2 lies on right side of Γ_1 then Γ_1 and Γ_2 can intersect or not. Generically, they have an even number of intersections (see Figure 4, right). The nature of a positive equilibrium F^* is stated in the following lemmas.

Lemma 4. *If an equilibrium $F^* = (x_1^*, x_2^*)$ exists, then it is a stable node if $F_1'(x_1^*) > F_2'(x_1^*)$. It is a saddle point if the opposite inequality is satisfied.*

The number of equilibria of (3) and their nature are summarized in the following theorem.

Theorem 1. *1. If $D < \min(D_1, D_2)$, then (3) admits the trivial equilibrium F^0 which is an unstable node, the boundary equilibria F^1 and F^2 which are saddle points, and at least one positive equilibrium F^*. If the positive equilibrium F^* is unique, then it is a stable node. Generically, the system has an odd number of positive equilibria which are alternatively stable nodes and saddle points. The one at the very left of these positive equilibria is a stable node.*

2. If $\min(D_1, D_2) < D < \max(D_1, D_2)$, four subcases must be distinguished:

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(a) *If $D_1 < D_2$ and $D_1 < D < D_4$, then (3) admits the trivial and boundary equilibria F^0 and F^2, which are saddle points, and at least one positive equilibrium F^*. If the positive equilibrium F^* is unique, then it is a stable node. Generically, the system has an odd number of positive equilibria which are alternatively stable nodes and saddle points. The one at the very left of these positive equilibria is a stable node.*

(b) *If $D_1 < D_2$ and $D_4 < D < D_2$, then (3) admits the trivial equilibrium F^0, which is a saddle point, and the boundary equilibrium F^2, which is a stable node. Generically, the system can have an even number of positive equilibria which are alternatively saddle points and stable nodes. The one at the very left of these positive equilibria is a saddle point.*

(c) *If $D_2 < D_1$ and $D_2 < D < D_3$, then (3) admits the trivial and boundary equilibria F^0 and F^1, which are saddle points, and at least one positive equilibrium F^*. If the positive equilibrium F^* is unique, then it is a stable node. Generically, the system has an odd number of positive equilibria which are alternatively stable nodes and saddle points. The one at the very left of these positive equilibria is a stable node.*

(d) *If $D_2 < D_1$ and $D_3 < D < D_1$, then (3) admits the trivial equilibrium F^0, which is a saddle point, and the boundary equilibrium F^1, which is a stable node. Generically, the system can have an even number of positive equilibria which are alternatively saddle points and stable nodes. The one at the very left of these positive equilibria is a saddle point.*

3. *If $D > \max(D_1, D_2)$, then (3) admits the trivial equilibrium F^0 which is a stable node. Generically, the system can have an even number of positive equilibria which are alternatively saddle points and stable nodes. The one at the very left of these positive equilibria is a saddle point.*

4. **Global analysis.** Let us first establish that (3) admits no periodic orbit nor polycycle inside $\mathcal{S}$.

Proposition 2. *There are no periodic orbits nor polycycles inside $\mathcal{S}$.*

Using the Butler MacGehee Theorem and Poincaré-Bendixon theory, we obtain the asymptotic behaviour of the reduced system (3).

Theorem 2. *Assuming that system (3) has at most one positive equilibrium F^*, then for every initial condition in $\mathcal{S}$, the trajectories of system (3) converge asymptotically to :*

- F^* *if* $D < \min(D_1, D_2)$.
- F^* *if* $D_1 < D_2$ *and* $D_1 < D < D_4$
- F^2 *if* $D_1 < D_2$ *and* $D_4 < D < D_2$.
- F^* *if* $D_2 < D_1$ *and* $D_2 < D < D_3$.
- F^1 *if* $D_2 < D_1$ *and* $D_3 < D < D_1$.
- F^0 *if* $\max(D_1, D_4) < D$.

Using Thieme's results [14] on asymptotically autonomous systems, we can deduce that the asymptotic behaviour of the solution of the complete system (2) is the same as the asymptotic behaviour described for the reduced system (3).

Theorem 3. *Assuming that system (3) has at most one positive equilibrium F^*, then for every initial condition in $\mathbb{R}^4_+$, the trajectories of system (2) converge asymptotically to:*

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- E^* *if* $D < \min(D_1, D_4)$.
- E^* *if* $D_1 < D_2$ *and* $D_1 < D < D_4$.
- E^2 *if* $D_1 < D_2$ *and* $D_4 < D < D_2$.
- E^* *if* $D_2 < D_1$ *and* $D_2 < D < D_3$.
- E^1 *if* $D_2 < D_1$ *and* $D_3 < D < D_1$.
- E^0 *if* $\max(D_1, D_2) < D$.

5. Applications.

5.1. **A particular case.** In this section we consider the case where $s_2^{in} = 0$ and f_2 depends only on s_2. We obtain the model

$$\begin{cases} \dot{s}_1 &= D(s_1^{in} - s_1) - f_1(s_1, s_2)x_1 \ , \\ \dot{x}_1 &= f_1(s_1, s_2)x_1 - Dx_1 \ , \\ \dot{s}_2 &= -Ds_2 - f_2(s_2)x_2 + f_1(s_1, s_2)x_1 \ , \\ \dot{x}_2 &= f_2(s_2)x_2 - Dx_2 \ , \end{cases} \tag{9}$$

considered in [7]. The assumptions about f_1 are the same as our assumptions. Assumption **H4** about f_2 becomes

H4: For all $s_2 \in \mathbb{R}_+$, $f_2'(s_2) > 0$.

The reduced system is

$$\begin{cases} \dot{x}_1 = \left[f_1\left(s_1^{in} - x_1, x_1 - x_2\right) - D\right] x_1, \\ \dot{x}_2 = \left[f_2\left(x_1 - x_2\right) - D\right] x_2. \end{cases} \tag{10}$$

Thus, for (10) the state-vector (x_1, x_2) belongs to (see Figure 5)

$$\mathcal{S} = \left\{(x_1, x_2) \in {\mathbb{R}_+}^2 : 0 < x_1 \leq s_1^{in}, 0 < x_2 \leq x_1\right\}.$$

Since $s_2^{in} = 0$ in (9), (7) becomes

$$D_1 = f_1(s_1^{in}, 0), \qquad D_2 = f_2(0) = 0.$$

Since $\Phi_1(x_1, 0) = f_1(s_1^{in} - x_1, x_1)$ and $\Phi_2(x_1, 0) = f_2(x_1)$, (8) gives the sole real number $D_3 \in]0, D_1[$ such that (see Figure 2, right):

$$f_1(s_1^{in} - \xi_1, \xi_1) = f_2(\xi_1) = D_3. \tag{11}$$

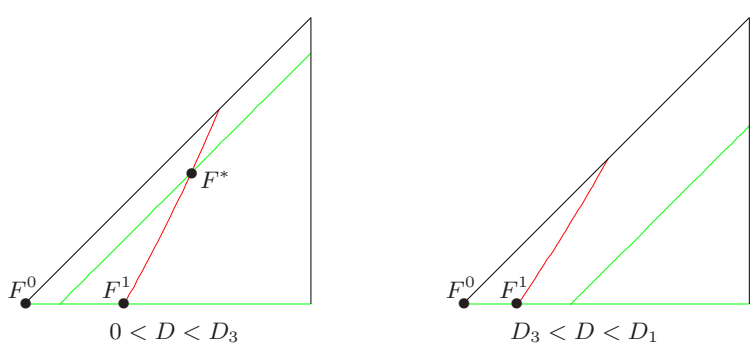

FIGURE 5. Relative positions of the isocline $\dot{x}_1 = 0$ (in red) and $\dot{x}_2 = 0$ (in green) for the reduced system (10). Multiple positive equilibria, as depicted on the center or on the right of Figure 4, cannot occur.

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If $D < D_1$ then equation $f_1(s_1^{in} - x_1, x_1) = D$ defines a sole number $\bar{x}_1$. As shown in Section 3, equation $f_1(s_1^{in} - x_1, x_1 - x_2) = D$ defines a function $x_2 = F_1(x_1)$ such that $F_1(\bar{x}_1) = 0$ when $D < D_1$. This function is increasing with derivative $F_1'(x_1) > 1$. On the other hand, equation $f_2(x_1 - x_2) = D$ defines the linear function $x_2 = x_1 - \lambda_2$, where $\lambda_2 = f_2^{-1}(D)$. Hence, the graphs Γ_1 and Γ_2 can intersect at most at one point: see Figure 5. The following proposition which gives the number and nature of equilibria of (10) is a consequence of Theorems 1 and 2.

Proposition 3. *1. If $D < D_3$, then (10) has three equilibria: F^0, which is an unstable node, F^1, which is a saddle point and F^*, which is a globally stable node.*
2. If $D_3 < D < D_1$, (10) has two equilibria: F^0, which is a saddle point, and F_1, which is a globally stable node.
3. If $D_1 < D$, then (10) has one equilibrium, F^0, which is a globally stable node.

Cases (1) and (2) of this Theorem correspond respectively to Theorems 3 and 4 of [7].

5.2. **Growth functions of generalized Monod type.** In this section we consider growth functions f_1 and f_2 of the following form

$$f_1(s_1, s_2) = \frac{m_1 s_1}{(K_1 + s_1)(L_1 + s_2)}, \qquad f_2(s_1, s_2) = \frac{m_2 s_1}{(K_2 + s_1)(L_2 + s_2)}. \tag{12}$$

Such functions are simply the product of a Monod function in s_1 by a decreasing function of s_2. Such functions are currently used in biotechnology when the growth of a functional species is limited by one substrate while inhibited by another. Such situations are common in water treatment technology such as the denitrification (limited by the nitrate and inhibited by the dissolved oxygen) or in anoxic or anaerobic hydrolysis (limited by the slowly-biodegradable substrates while inhibited by an excess of oxygen), processes which can be modeled this way (cf. [15]).

One can easily check that (12) satisfy Assumptions **H1** to **H4**. Straightforward calculations give

$$\begin{aligned} F_1(x_1) &= \frac{-Dx_1^2 + m_1 + D\big(K_1 - L_1 + s_1^{in} - s_2^{in}\big) - m_1 s_1^{in} + D\big(K_1 + s_1^{in}\big)\big(L_1 + s_2^{in}\big)}{D(K_1 + s_1^{in} - x_1)} \\ F_2(x_1) &= \frac{Dx_1^2 + m_2 + D\big(L_2 - K_2 + s_2^{in} - s_1^{in}\big) + m_2 s_2^{in} - D\big(K_2 + s_1^{in}\big)\big(L_2 + s_2^{in}\big)}{m_2 - D(K_2 + s_1^{in} - x_1)} \end{aligned}$$

Hence equation $F_1(x_1) = F_2(x_1)$, giving the abscissa of positive equilibria, is an algebraic equation of degree 2. Thus, it cannot have more than two solutions. Therefore, the situation shown in the center of Figure 4 with three positive equilibria, is excluded. However, the situation depicted on the right in Figure 4, showing two positive equilibria, can occur. For instance, consider the following values of the parameters:

$$m_1 = 8, \quad m_2 = 4, \quad K_1 = L_2 = 1, \quad L_1 = K_2 = 2, \quad s_1^{in} = s_2^{in} = 3. \tag{13}$$

Then

$$D_1 = 6/5, \qquad D_3 = 8/9, \qquad D_2 = 3/5.$$

There is another bifurcation value, $D = 1$, which correspond to the case when the graphs Γ_1 and Γ_2 are tangent: see Figure 7. For this example, five cases can occur (see Figure 6):

Proposition 4. *Consider system (3) where f_1 and f_2 are given by (12) with parameters (13).*

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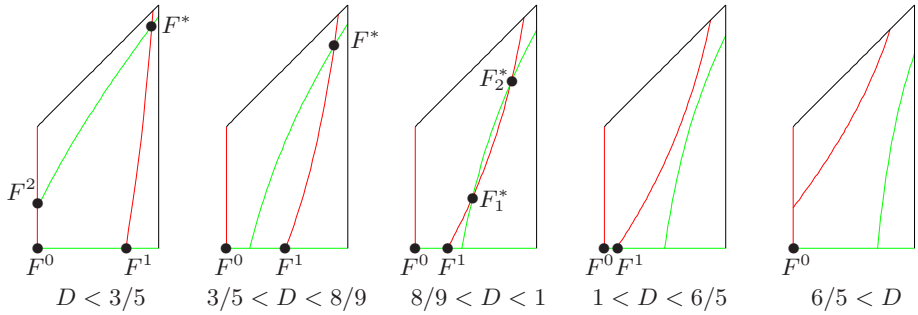

FIGURE 6. Relative positions of the isocline $\dot{x}_1 = 0$ (in red) and $\dot{x}_2 = 0$ (in green).

1. *If $D < 3/5$, then the system has four equilibria: F^0 which is an unstable node, F^1 and F^2, which are saddle points, and F^*, which is a stable node.*
2. *If $3/5 < D < 8/9$, then the system has three equilibria: F^0 and F^1, which are saddle points and F^*, which is a stable node.*
3. *If $8/9 < D < 1$, then the system has four equilibria: F^0 and F_1^*, which are saddle points and F^1 and F_2^*, which are stable nodes.*
4. *If $1 < D < 6/5$, then the system has two equilibria: F^0, which is a saddle point, and F^1 which is a stable node.*
5. *If $D > 6/5$, then the system has one equilibrium: F^0, which is a stable node.*

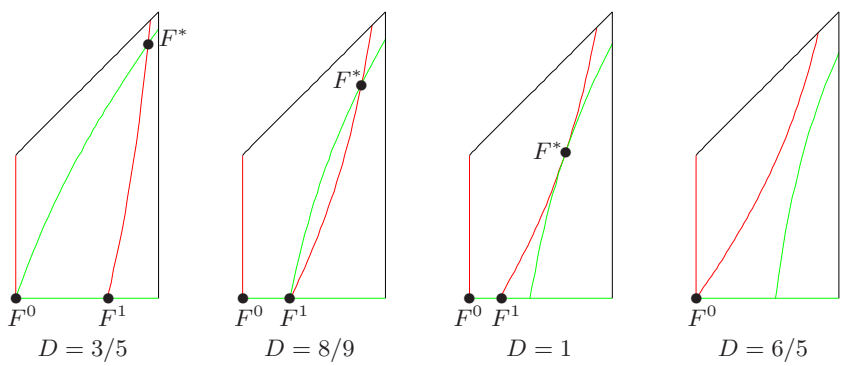

FIGURE 7. The non-hyperbolic cases. When $D = 6/5$, F^0 and F^2 coalesce. When $D = 8/9$, F_1^* and F^1 coalesce (saddle node bifurcation). When $D = 1$, F_1^* and F_2^* coalesce (saddle node bifurcation). When $D = 6/5$, F^0 and F^2 coalesce.

5.3. **Numerical simulations of the bistability case.** Consider system (3) where f_1 and f_2 are given by (12) with parameters (13). According to Proposition 4, in the case when $8/9 < D < 1$, a bistability phenomenon occurs. According to the initial condition, both species can coexist at equilibrium F_2^*, or species x_2 goes to extinction at equilibrium F^1. This phenomenon is illustrated numerically, with $D = 0.95$, in Figure 8.

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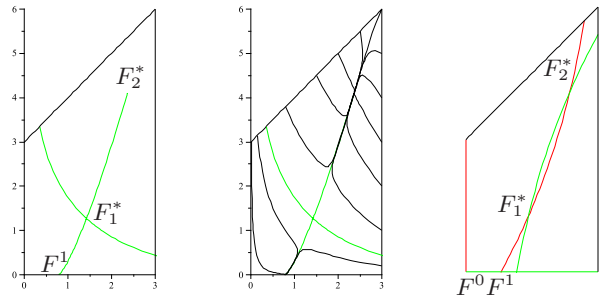

FIGURE 8. Numerical solutions in the bistability case $D = 0.95$ and parameter values (13). On the left, the separatrix (in green) of the saddle point F_1^* separate the domain $\mathcal{S}$ into two regions which are the basins of attraction of the boundary equilibrium point F^1 and the positive equilibrium point F_2^*. In the center, the phase portrait. On the right, the isoclines.

Consider again system (3) where f_1 and f_2 are given by (12) with parameters now given by

$$m_1 = 8, \quad m_2 = 7, \quad K_1 = K_2 = L_2 = 1, \quad L_1 = 3/2, \quad s_1^{in} = s_2^{in} = 3. \tag{14}$$

The bifurcation values are $D_1 = 4/3$ and $D_2 = 21/16$. If $D > \max(D_1, D_2)$, for instance for $D = 3/2$, one obtains a bistability phenomenon corresponding to case (3) of Theorem 1, with two positive equilibria. Depending on the initial conditions, both species can coexist at equilibrium F_2^*, or both species go to extinction at equilibrium F^0. This phenomenon is illustrated numerically in Figure 9.

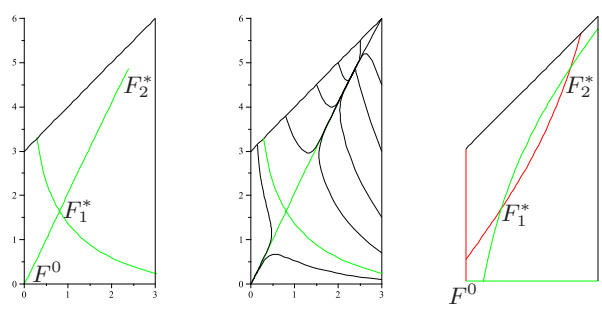

FIGURE 9. Numerical solutions in the bistability case $D = 1.5$ and parameters values (14). On the left, the separatrix (in green) of the saddle point F_1^* separate the domain $\mathcal{S}$ in two region which are the basins of attraction of the boundary equilibrium point F^0 and the positive equilibrium point F_2^*. On the center, the phase portrait. On the right, the isoclines.

6. **Conclusions.** We have proposed a mathematical model involving a syntrophic relationship of two bacteria. More precisely, we have considered a model of an ecosystem involving two bacteria in a chemostat where there are two resources in

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the input. For one of the populations, one resource is needed for growth and the other is inhibitory; for the other population, in contrast, the roles of the resources are reversed. One of the populations produces as a by-product the resource that is inhibitory to itself but needed for growth by the other population. The analysis of this model predicts that, under general and natural assumptions of monotonicity on the functional responses, the stable asymptotic coexistence of the two bacteria is possible. Extending the model studied in [7] by considering that there may have some S_2 in the influent and using a more general class of kinetics functions, we show that the qualitative behavior of the system can be significantly modified. In particular, if $S_2^{in} > 0$, the situation where X_1 is washed out but where $X_2 > 0$ is possible. In addition, positing the possible inhibition of the growth of X_2 by S_1 yields bistability. This work offers the perspective of providing an "elegant" formulation for synthesizing all results concerning the analysis of two-steps models of bioprocesses currently used for monitoring and control purposes.

Appendix A. The anaerobic digestion process : An example of a synthrophic relationship.

"Methane fermentation" or "anaerobic digestion" is a process that converts organic matter into a gaseous mixture composed mainly of methane and carbon dioxide (CH_4 and CO_2) through the action of a complex bacterial ecosystem (cf. Fig.10). It is often used for the treatment of concentrated wastewaters or to convert the excess sludge produced in wastewater treatment plants into more stable products. There is also considerable interest in digesters fed with plant biomass, since the methane produced can be used profitably as a source of energy. It is usually considered that a number of metabolic groups of bacteria are involved sequentially in the fermentation process.

One specific characteristic of the anaerobic process is that within the involved groups of bacteria, there exist populations exhibiting obligatory mutualistic relationships. Such a syntrophic relationship is necessary for the biological reactions to be thermodynamically possible. In the first stages of the reactions (which together are called "acidogenesis"), some hydrogen is produced. However, in El Hajji et al.[7], this production of hydrogen at this stage was ignored (compare Fig.10 with Fig.1 of [7]). This hypothesis constitutes the first novelty with respect to [7]. It is to be noticed that an excess of hydrogen in the medium inhibits the growth of another bacterial group called "acetogenic bacteria". Their association with H_2-consuming bacteria is thus necessary for the second stage of the reaction to occur. Such a syntrophic relationship has been pointed out in a number of experimental works (cf. for instance the seminal work by [4]). Let us consider the subsystem of the anaerobic system where the VFA (for Volatile Fatty Acids) are transformed into H_2, CH_4 and $CO2$. The corresponding biological reactions can be formalized as a first bacterial consortium X_1 (the acetogens) transforming S_1 (the VFA) into S_2 (the hydrogen) and acetate (cf. Fig.10). Then, a second species X_2 (the hydrogenotrophic-methanogenic bacteria) grows on S_2. In practice, acetogens are inhibited by an excess of hydrogen and methanogens by an excess of VFA. Thus, it is further assumed that X_1 is inhibited by S_2 and X_2 by S_1. The last inhibiting relationship constitutes the second innovation with respect to [7].
This situation is precisely that dealt with by the model (1).

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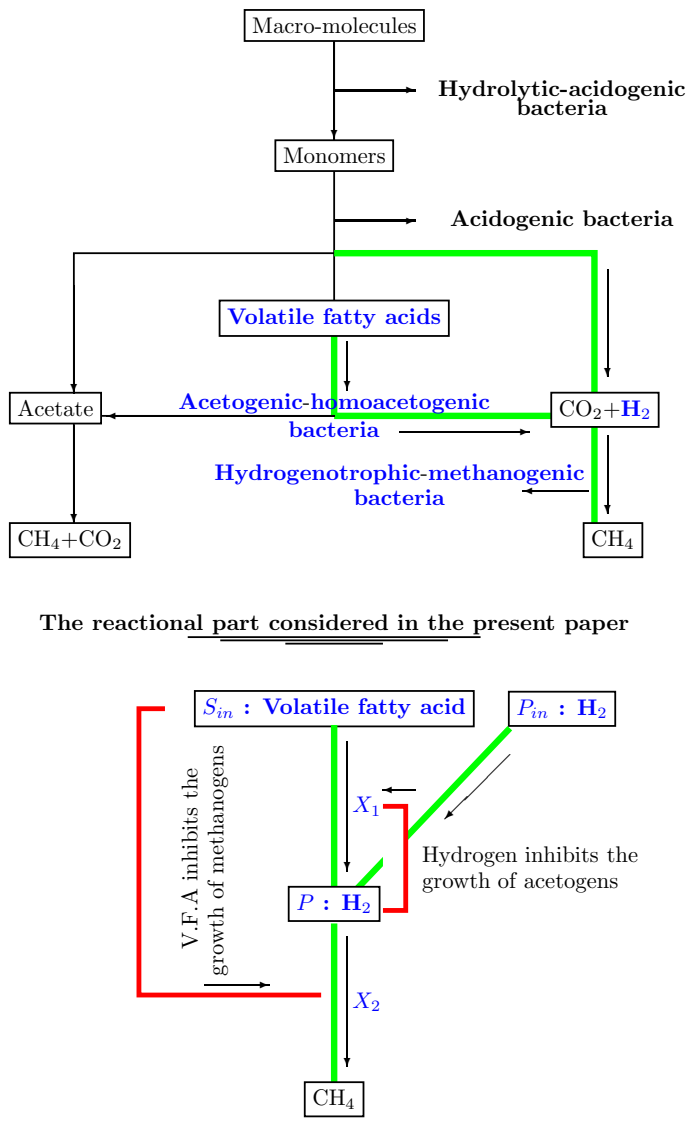

FIGURE 10. Anaerobic fermentation process

Appendix B. Proofs.

Proof of Proposition 1. The invariance of $\mathbb{R}^4_+$ is guaranteed by the fact that :

i. $s_1 = 0 \Rightarrow \dot{s}_1 = D\, s_1^{in} > 0$,
ii. $s_2 = 0 \Rightarrow \dot{s}_2 = D\, s_2^{in} + f_1(s_1, 0)\, x_1 > 0$,
iii. $x_i = 0 \Rightarrow \dot{x}_i = 0$ for $i = 1, 2$.

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Next, it must be proved that the solution is bounded. Let $z_1 = s_1 + x_1$, then $\dot{z}_1 = -D(z_1 - s_1^{in})$ from which it follows that :

$$s_1(t) + x_1(t) = s_1^{in} + (s_1(0) + x_1(0) - s_1^{in})e^{-Dt} \ . \tag{15}$$

Thus $s_1(t)$ and $x_1(t)$ are positively bounded. Let $z_2 = s_2 + x_2 - x_1$, then $\dot{z}_2 = -D(z_2 - s_2^{in})$ from which it can be deduced that:

$$s_2(t) + x_2(t) - x_1(t) = s_2^{in} + (s_2(0) + x_2(0) - x_1(0) - s_2^{in})e^{-Dt} \ . \tag{16}$$

Thus $s_2(t)$ and $x_2(t)$ are positively bounded. Hence, the solution is defined for all positive t. From (15) and (16), it can be deduced that the set Ω is an invariant set which is an attractor. □

Proof of Lemma 1. The Jacobian matrix J of (3), at point (x_1, x_2), is given by:

$$J = \begin{bmatrix} -\dfrac{\partial f_1}{\partial s_1}x_1 + \dfrac{\partial f_1}{\partial s_2}x_1 + f_1 - D & -\dfrac{\partial f_1}{\partial s_2}x_1 \\ -\dfrac{\partial f_2}{\partial s_1}x_2 + \dfrac{\partial f_2}{\partial s_2}x_2 & -\dfrac{\partial f_2}{\partial s_2}x_2 + f_2 - D \end{bmatrix}.$$

where the functions are evaluated at $\left(s_1^{in} - x_1, s_2^{in} + x_1 - x_2\right)$. The Jacobian matrix at F^0 is given by:

$$J^0 = \begin{bmatrix} f_1(s_1^{in}, s_2^{in}) - D & 0 \\ 0 & f_2(s_1^{in}, s_2^{in}) - D \end{bmatrix}$$

The eigenvalues are $D_1 - D$ and $D_2 - D$. Thus, if $D > \max(D_1, D_2)$, then F^0 is a stable node. It is an unstable node if $D < \min(D_1, D_2)$. It is a saddle point if $\min(D_1, D_2) < D < \max(D_1, D_2)$. □

Proof of Lemma 2. An equilibrium $F^1 = (\bar{x}_1, 0)$ exists if and only if $x_1 = \bar{x}_1 \in]0, s_1^{in}[$ is a solution of (4). Let $\psi_1(x_1) = \Phi_1(x_1, 0)$. Then

$$\psi_1'(x_1) = -\frac{\partial f_1}{\partial s_1}(s_1^{in} - x_1, s_2^{in} + x_1) + \frac{\partial f_1}{\partial s_2}(s_1^{in} - x_1, s_2^{in} + x_1).$$

By assuming **H3**, $\psi_1'(x_1) < 0$. Since $\psi_1(0) = D_1$, and $\psi_1(s_1^{in}) = 0$, equation (4) admits a solution in the interval $]0, s_1^{in}[$ if and only if $D < D_1$. If this condition is satisfied then (4) admits one single solution since the function $\psi_1(.)$ is decreasing (see Figure 2). The Jacobian matrix at F^1 is given by:

$$J^1 = \begin{bmatrix} -\dfrac{\partial f_1}{\partial s_1}\bar{x}_1 + \dfrac{\partial f_1}{\partial s_2}\bar{x}_1 & -\dfrac{\partial f_1}{\partial s_2}\bar{x}_1 \\ 0 & f_2 - D \end{bmatrix}$$

where the functions are evaluated at $(s_1^{in} - \bar{x}_1, s_2^{in} + \bar{x}_1)$. The eigenvalues are

$$f_2(s_1^{in} - \bar{x}_1, s_2^{in} + \bar{x}_1) - D = \Phi_2(\bar{x}_1, 0) - D, \text{ and } -\frac{\partial f_1}{\partial s_1}\bar{x}_1 + \frac{\partial f_1}{\partial s_2}\bar{x}_1 < 0.$$

Thus F^1 is a saddle point if $\Phi_2(\bar{x}_1, 0) > D$. If $D_1 < D_2$, this condition is satisfied for all $D < D_1$. If $D_2 < D_1$, it is satisfied for all $0 < D < D_3$ (see Figure 2). F^1 is a stable node if $D_3 < D < D_1$ and $D_2 < D_1$. □

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Proof of Lemma 3. An equilibrium $F^2 = (0, \tilde{x}_2)$ exists if and only if $x_2 = \tilde{x}_2 \in]0, s_2^{in}[$ is a solution of (5). Let $\psi_2(x_2) = \Phi_2(0, x_2)$. Then

$$\psi_2'(x_2) = -\frac{\partial f_1}{\partial s_2}(s_1^{in}, s_2^{in} - \tilde{x}_2).$$

By assuming **H4**, $\psi_2'(x_2) < 0$. Since $\psi_2(0) = D_2$, and $\psi_2(s_2^{in}) = 0$, equation (5) admits a solution in the interval $]0, s_2^{in}[$ if and only if $D < D_2$. If this condition is satisfied, then (5) admits one single solution since the function $\psi_2(.)$ is decreasing (see Figure 3). The Jacobian matrix at F^2 is given by:

$$J^2 = \begin{bmatrix} f_1 - D & 0 \\ -\frac{\partial f_2}{\partial s_1}\tilde{x}_2 + \frac{\partial f_2}{\partial s_2}\tilde{x}_2 & -\frac{\partial f_2}{\partial s_2}\tilde{x}_2 \end{bmatrix}$$

where the functions are evaluated at $(s_1^{in}, s_2^{in} - \tilde{x}_2)$. The eigenvalues are

$$f_1(s_1^{in}, s_2^{in} - \tilde{x}_2) - D = \Phi_1(0, \tilde{x}_2) - D, \text{ and } -\frac{\partial f_2}{\partial s_2}\tilde{x}_2 < 0.$$

Thus F^2 is a saddle point if $\Phi_1(0, \tilde{x}_2) > D$. If $D_2 < D_1$, this condition is satisfied for all $D < D_2$. If $D_1 < D_2$, it is satisfied for all $0 < D < D_4$ (see Figure 3). F^2 is a stable node if $D_4 < D < D_2$ and $D_1 < D_2$. □

Proof of Lemma 4. The Jacobian matrix at F^* is given by:

$$J^* = \begin{bmatrix} -\frac{\partial f_1}{\partial s_1}x_1^* + \frac{\partial f_1}{\partial s_2}x_1^* & -\frac{\partial f_1}{\partial s_2}x_1^* \\ -\frac{\partial f_2}{\partial s_1}x_2^* + \frac{\partial f_2}{\partial s_2}x_2^* & -\frac{\partial f_2}{\partial s_2}x_2^* \end{bmatrix}$$

where the derivatives are evaluated at $(s_1^{in} - x_1^*, s_2^{in} + x_1^* - x_2^*)$. Notice that

$$\mathrm{tr}(J^*) = -\frac{\partial f_1}{\partial s_1}x_1^* + \frac{\partial f_1}{\partial s_2}x_1^* - \frac{\partial f_2}{\partial s_2}x_2^* < 0$$

and

$$\det(J^*) = x_1^* x_2^* \left[\frac{\partial f_1}{\partial s_1}\frac{\partial f_2}{\partial s_2} - \frac{\partial f_1}{\partial s_2}\frac{\partial f_2}{\partial s_1}\right] = x_1^* x_2^* \frac{\partial f_1}{\partial s_2}\frac{\partial f_2}{\partial s_2}\left[F_2'(x_1^*) - F_1'(x_1^*)\right].$$

Given assumptions **H3** and **H4**, the product of the partial derivatives is negative. Therefore, the determinant is positive if $F_1'(x_1^*) > F_2'(x_1^*)$ and negative otherwise. Hence, the equilibrium $F^* = (x_1^*, x_2^*)$ is a stable node if $F_1'(x_1^*) > F_2'(x_1^*)$ and a saddle point otherwise. □

Proof of Theorem 1. We give the details of the proof in the case where

$$D < \min(D_1, D_2) \text{ or } D > \max(D_1, D_2).$$

The other cases can be proved similarly. The washout equilibrium point F_0 always exists. According to Lemma 1, it is an unstable node if $D < \min(D_1, D_2)$ and a stable node for $D > \max(D_1, D_2)$.

Consider first the case $D < \min(D_1, D_2)$. Lemmas 2 and 3 show that the system admits two boundary equilibria F_1 and F_2, which are saddle points. Since Γ_2 starts on the left side of Γ_1 and ends on its right, the graphs Γ_1 and Γ_2 have at least one intersection. In the generic case, where all intersections are transverse, the graphs can have an odd number of intersections (see Figure 4, center). According

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Doi : 10.3934/mbe.2012.9.627

to Lemma 4, these intersections are alternatively saddle points and stable nodes. The one at the very left of these positive equilibria is a stable node since at this point the condition $F_1'(x_1^*) > F_2'(x_1^*)$ is satisfied.

Consider now the case $D > \max(D_1, D_2)$. Lemmas 2 and 3 show that the system admits no boundary equilibria F_1 and F_2. Since Γ_2 starts and ends on the right side of Γ_1, the graphs Γ_1 and Γ_2 can either intersect or not. In the generic case, where all intersections are transverse, the graphs can have an even number of intersections (see Figure 4, right). According to Lemma 4, these intersection are alternatively saddle points and stable nodes. The one at the very left of these positive equilibria is a saddle point since at this point the condition $F_1'(x_1^*) < F_2'(x_1^*)$ is satisfied. □

Proof of Proposition 2. Consider a trajectory of (3) belonging to $\mathcal{S}$. Let us transform the system (3) through the change of variables $\xi_1 = \ln(x_1)$, $\xi_2 = \ln(x_2)$. Then one obtains the following system:

$$\left\{\begin{array}{rcl} \dot{\xi_1} & = & h_1(\xi_1, \xi_2) := f_1(s_1^{in} - e^{\xi_1}, s_2^{in} + e^{\xi_1} - e^{\xi_2}) - D, \\ \dot{\xi_2} & = & h_1(\xi_1, \xi_2) := f_2(s_1^{in} - e^{\xi_1}, s_2^{in} + e^{\xi_1} - e^{\xi_2}) - D. \end{array}\right. \tag{17}$$

This gives

$$\frac{\partial h_1}{\partial \xi_1} + \frac{\partial h_2}{\partial \xi_2} = -e^{\xi_1}\frac{\partial f_1}{\partial s_1} + e^{\xi_1}\frac{\partial f_1}{\partial s_2} - e^{\xi_2}\frac{\partial f_2}{\partial s_2} < 0.$$

From the Dulac criterion [13], it can be deduced that the system (17) has no periodic trajectory. Hence (3) has no periodic orbit in $\mathcal{S}$. □

Proof of Theorem 2. We give the details of the proof in the case when

$$D < \min(D_1, D_2).$$

The other cases can be proved similarly. Let $x_1(0) > 0, x_2(0) > 0$ and ω the ω-limit set of $(x_1(0), x_2(0))$. ω is an invariant compact set and $\omega \subset \bar{\mathcal{S}}$. Assume that ω contains a point M on the x_1x_2 axis :

- M cannot be F^0 because F^0 is an unstable node and cannot be a part of the ω-limit set of $(x_1(0), x_2(0))$,
- If $M \in]\bar{x}_1, s_1^{in}] \times \{0\}$ (respectively $M \in \{0\}\times]\bar{x}_2, s_2^{in}]$). As ω is invariant then $\gamma(M) \subset \omega$, which is impossible because ω is bounded and $\gamma(M) =]\bar{x}_1, +\infty[\times\{0\}$ (respectively $\gamma(M) = \{0\}\times]\bar{x}_2, +\infty[$),
- If $M \in]0, \bar{x}_1[\times\{0\}$ (respectively $M \in \{0\}\ ,\times]0, \bar{x}_2[$). ω contains $\gamma(M) =]0, \bar{x}_1[\times\{0\}$ (respectively $\gamma(M) = \{0\}\times]0, \bar{x}_2[$). As ω is a compact, then it contains the adherence of $\gamma(M)$, $[0, \bar{x}_1] \times \{0\}$ (respectively $\{0\} \times [0, \bar{x}_2]$). In particular, ω contains F^0 which is impossible,
- If $M = F^1$ (respectively $M = F^2$). ω is not reduced to F^1 (respectively to F^2). By the Butler-McGehee theorem, ω contains a point P of $(0, +\infty) \times \{0\}$ other than F^1 (respectively of $\{0\} \times (0, +\infty)$ other than F^2), which is impossible.

Finally, the ω-limit set does not contain any point on the x_1x_2 axis. System (3) has no periodic orbit inside $\mathcal{S}$. Using the Poincaré-Bendixon Theorem [13], F^* is a globally asymptotically stable equilibrium point for system (3). □

Proof of Theorem 3. Let $(s_1(t), x_1(t), s_2(t), x_2(t))$ be a solution of (2). From (15) and (16) it can be deduced that

$$s_1(t) = s_1^{in} - x_1(t) + K_1e^{-Dt} \quad \text{and} \quad s_2(t) = s_2^{in} + x_1(t) - x_2(t) + K_2e^{-Dt},$$

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Doi : 10.3934/mbe.2012.9.627

where $K_1 = s_1(0) + x_1(0) - s_1^{in}$ and $K_2 = s_2(0) + x_2(0) - x_1(0) - s_2^{in}$. Hence $(x_1(t), x_2(t))$ is a solution of the nonautonomous system of two differential equations

$$\begin{cases} \dot{x}_1 &= \left[f_1\left(s_1^{in} - x_1 + K_1 e^{-Dt}, s_2^{in} + x_1 - x_2 + K_2 e^{-Dt}\right) - D\right] x_1, \\ \dot{x}_2 &= \left[f_2\left(s_1^{in} - x_1 + K_1 e^{-Dt}, s_2^{in} + x_1 - x_2 + K_2 e^{-Dt}\right) - D\right] x_2. \end{cases} \tag{18}$$

This is an asymptotically autonomous differential system which converge towards the autonomous system (3). The set Ω is an attractor of all trajectories in $\mathbb{R}_+^4$ and the phase portrait of system reduced to Ω (3) contains only locally-stable nodes, unstable nodes, saddle points and no trajectory joining two saddle points. Thus Thiemes's results [14] can be applied and the conclusion reached that the asymptotic behaviour of the solution of the complete system (18) is the same as the asymptotic behaviour described for the reduced system (3): the main result can then be deduced. □

Proof of Proposition 3. Global attractivity follows from Theorem 2.
1. If $D < D_3$ then case (2.c) of Theorem 1, with one single positive equilibrium, holds.
2. If $D_3 < D < D_1$, then (2.d) of Theorem 1, with two positive equilibria, holds.
3. If $D > D_1$, then case (3) of Theorem 1, with no positive equilibrium, holds. □

Proof of Proposition 4. Global attractivity follows from Theorem 2.
1. If $D < 3/5$ then case (1) of Theorem 1, with one single positive equilibrium, holds.
2. If $3/5 < D < 8/9$, then case (2.c) of Theorem 1, with one single positive equilibrium, holds.
3. If $8/9 < D < 1$, then case (2.d) of Theorem 1, with two positive equilibria, holds.
4. If $1 < D < 6/5$, then case (2.d) of Theorem 1, with no positive equilibrium, holds.
5. If $D > 6/5$, then case (3) of Theorem 1, with no positive equilibrium, holds. □

Acknowledgements. We thank the anonymous referees for their valuable comments and suggestions. This research has been partially funded by the French ANR project DISCO (2010-2012) of the SYSCOMM program.

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Received November 8, 2011; Accepted April 16, 2012.

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